Clinical Trials – The role of Pharmacy

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Objectives

- Why is pharmacy required in clinical trials?
- What does pharmacy do and why?
- How can you help?
- Additional roles
Why involve pharmacy?

- Pharmacy has a vital role in relation to clinical research, which is to **safeguard** participants, healthcare professionals and the Trust by ensuring Investigational Medicinal Products (IMP’s) are **appropriate for use** and are procured, handled, stored and used **safely** and **correctly**.
Before the Trial
Protocol

• Review the clinical trial protocol:
  • Is the dose appropriate for all trial participants?
  • Are all contra-indications listed in exclusion criteria?
  • Are all drug/disease interactions listed in exclusion criteria?
  • Have all expected side effects been included in protocol/patient information leaflet?
Review of trial protocol

• Discuss any protocol omissions or issues that need clarifying with Sponsor or Investigator
• Request a copy of the manufacturing and/or import authorisation to ensure that IMP manufactured/imported in compliance with Directive
• When all issues clarified and protocol amended (if necessary) trial can be approved from pharmacy perspective
Legalities

- Will the IMP be manufactured or imported under the terms of a manufacturing authorisation?
- IMPs must be manufactured to good manufacturing practice (GMP)
- Manufacturer must have a manufacturing licence
  - Protects against poor quality or badly prepared medicines
- Will the IMP be labelled in accordance with annex 13 (GMP)
Regulation 13

• Supply of investigational products for the purposes of clinical trials

• (1) Subject to paragraphs (3) and (4), no person shall, in the course of a business carried on by him, sell or supply any IMP to:
  • an investigator
  • a health care professional who is a member of an investigators team
  • a person who provides or is to provide health care under the direction or control of a person referred to above
  • a subject

For the purpose of administering that product in a clinical trial, unless the conditions specified in paragraph (2) are satisfied
The conditions referred to in paragraph (1) are:

• the licensing authority has authorised the clinical trial for the purposes of which the product is sold or supplied

• in the case of an IMP manufactured or assembled in an EEA State, other than in accordance with the terms of a marketing authorization relating to that product, or imported into an EEA state-

• the product has been manufactured, assembled or imported in accordance with the terms of:

  • a manufacturing authorisation, or

  • an authorisation referred to in Article 13 of the Directive granted by a competent authority of an EEA state other than the United Kingdom, and

• the production batch of IMP of which the product is a part has been checked and certified by a qualified person pursuant to Article 13(3) and (4) of the Directive
**Regulation 46 - Labelling of IMP**

- An IMP shall be labelled in accordance with Art 15 of commission directive 2003/94/EC
- Paragraph (1) shall not apply where the IMP is:
  - for use in a clinical trial with the characteristics specified in the second paragraph of article 14 of the Directive
  - dispensed to a subject in accordance with a prescription given by a health care professional, and
  - labelled in accordance with the requirements of Schedule 5 to the Medicines for Human Use (Marketing Authorisation etc) Regulation 1994 that apply in relation to dispensed relevant medicinal product
Practicalities

- Do we have the facilities required for the trial?
  - Aseptic preparation?
  - Storage?

- Does the IMP pose a risk to staff?
  - Cytotoxic
  - Handling precautions

- Is the trial blinded?
  - Unblinding procedures
Finances

• Costing Template
  • Are all services accounted for?
  • Are the theoretical activity times realistic?
  • Do standard prescription charges apply?
  • Extra charges e.g. excess storage, drug destruction
Trial Approval

Before a clinical trial can be started and IMP dispensed pharmacy must be satisfied that there is:

- Clinical Trial Authorisation from the MHRA (and all remarks on approval letter have been answered)
- Ethics committee approval for Trial and Individual Site
- Local R&D department approval
- A signed contract between Sponsor and Trust that includes a section on IMP that pharmacy can comply with
Following trial approval

• Trial specific dispensing procedures and trial summary
  • Dispensing procedure checked and approved by clinical trials pharmacist

• Staff training

• Initiation meeting with trial sponsor/investigator
  • review pharmacy trial file
  • Agree prescription, accountability log and other trial documents
  • finalise arrangements for IMP delivery, receipt and storage
  • discuss any special requirements for trial dispensing
During the trial
IMP receipt

- Check temperature on any monitoring devices with delivery
  - If out of range follow instructions with device and quarantine IMP
- Reconcile items delivered with delivery note
  - Notify supplier of any discrepancies
- Ensure QP (IMP) release statement and Certificate of Analysis held in pharmacy for each batch of IMP delivered
  - Quarantine IMP if not present
- Acknowledge shipment as instructed on delivery note
IMP storage

- IMPs should be delivered directly to the pharmacy department

- IMP should be stored separately from normal pharmacy stock in area with restricted access
  - not stored on ward/clinic area unless used in emergency care

- Returned or expired IMP should be stored separately from unused IMP

- Regular temperature monitoring
  - Temperature deviations reported to CRA and medication quarantined
IMP Dispensing

- PI (or delegated Doctor) prescribe IMP on drug chart/prescription
- Signed prescription sent to pharmacy for dispensing
- Bloods etc checked if required
- IMP taken from dedicated IMP storage area
- Temperature checked to ensure in range
- If outside of range IMP must not be used
- Medication prepared
Labelling

**Directive 2003/94/EC – Article 15 Labelling**
- In the case of an IMP, labelling should be such as:
  - to ensure the protection of the subject
  - to enable identification of the product and trial
  - To facilitate the proper use of the IMP
  - All IMP need to be labelled in accordance with GMP (Annex 13)

**Pharmacy**
- Patient initials and subject number
- Medication
- Administration instructions
- “keep out of sight and reach of children”
- Address of pharmacy
Accountability

- Accountability form completed when medication removed
  - Number of products issued
  - Batch number and expiry date
  - Patient initials and trial number
  - Signature of person dispensing and checking medication
IMP dispensing

- All staff dispensing and checking IMP must be trained in GCP and procedures for dispensing IMP.
- Trial specific dispensing procedures should be followed by all staff dispensing and checking IMP.
- IMP should only be dispensed on receipt of a prescription signed by the Investigator or delegated prescriber.
- IMP accountability logs are completed when IMP dispensed.
IMP Dispensing Time

- Notice needs to be given in advance of prescriptions being sent to pharmacy.
  - 30 minutes allowed for outpatient prescriptions in this Trust
  - More paperwork required for Trial prescriptions

- Prescriptions can be prepared in advance of appointment
  - Saves patient time
  - Ensures medication is ready when needed
IMP returns

• All used or unused IMPs should be returned to pharmacy

• On return medication should be checked to determine the quantity and this should be logged in the accountability records

• Medication can be destroyed from pharmacy or sent back for destruction
  • Must be checked by CRA
End of a trial
Filing and accountability

• Ensure all documentation is accurate
• Everything filed in Pharmacy Folder
• End of trial monitoring visit
• Marry PSF and SF together
Other pharmacy roles during trial
Emergency unblinding

- Code breaks
  - Is unblinding actually necessary?
  - Who can unblind?
  - Who is blinded/unblinded?
  - Where are code breaks kept?
Other Pharmacist roles

- Notify investigator and/or sponsor if subject admitted to hospital or reports adverse reaction
- IMP recall
- Monitoring visits and audits
- Principal Investigator
Summary

• To **safeguard** subjects, healthcare professionals and the Trust by ensuring IMP are appropriate for use and are procured, handled, stored and used safely and correctly

• To ensure that IMP are managed and dispensed to patients in accordance with the **protocol**

• To ensure that all pharmacy clinical trial procedures comply with relevant **guidelines** and **regulations**